REMARKS

Claims 4-7 are pending. Applicants have cancelled claim 7 without prejudice and added claims 9-15. Claims 4-6 and 9-15 will therefore be pending upon entry of the proposed amendments.

Claims 4 and 5 have been amended as follows. Applicants have removed the phrase "or inhibiting" and deleted "O" (oxygen) from the listing of permissible values for variable Y. As such, claims 4 and 5 as currently amended require that the administered compound is a compound of formula (I) in which Y is S, NH, NMe, or CH_2. In view of the foregoing, Applicants have also removed the proviso at the end of each claim, as this proviso applies to compounds in which "Y is O." Support for these amendments can be found throughout the Specification, e.g., at page 4, line 4 and page 17, lines 4-6.

New independent claims 9 and 10 are directed to methods for the prevention of "hyperproliferative vascular disorders following vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation in a mammal in need thereof" and methods for the prevention of "restenosis following vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation in a mammal in need thereof," respectively. As suggested by the Examiner, claims 9 and 10 recite the gerund "preventing" instead of the gerund "inhibiting." New claims 9 and 10 also require that the administered compound is a compound of formula (I) in which Y is S, NH, NMe, or CH_2. Support for these amendments can be found throughout the Specification, e.g., at page 4, line 4 and page 17, lines 6-12 and claim 6 as originally filed.

New independent claims 11 and 12 are directed to methods for the treatment of "hyperproliferative vascular disorders" and "restenosis," respectively. New dependent claim 13 includes the subject matter of claim 6 as originally filed. New independent claims 14 and 15 are directed to methods for the prevention of "hyperproliferative vascular disorders following vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation in a mammal in need thereof" and methods for the prevention of "restenosis

following vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation in a mammal in need thereof," respectively. New claims 11-15 require that the administered compound must be selected from the group consisting of:

N-{5-[(Hepta-*O*-acetyl-β-D-maltosyloxy)-methyl]-2-chloro-phenyl}-L-aspartamide-γ-*tert*- butyl ester or a pharmaceutically acceptable salt thereof;

N-{2-Chloro-5-[(2,2',3,3',4',6,6')-hepta-*O*-acetyl-β-D-maltosyl-oxymethyl]-phenyl}- (9*H*-fluoren-9-ylmethoxycarbonyl)-L-alaninamide or a pharmaceutically acceptable salt thereof;

4-Benzoyl-*N*-{2-chloro-5-[(2,2',3,3',4',6,6'-hepta-*O*-acetyl-β-D-maltosyl)-oxy-methyl]- phenyl}-benzamide or a pharmaceutically acceptable salt thereof;

N-[2-Chloro-5-(β-D-maltosyl-oxymethyl)-phenyl]-acetamide or a pharmaceutically acceptable salt thereof;

N-{5-[6,6'-Di-*O*-(*tert*-butyl-dimethyl-silyl)-β-D-maltosyloxy-methyl]-2-methyl-phenyl}- acetamide or a pharmaceutically acceptable salt thereof;

N-{2-Chloro-5-[6,6'-di-*O*-(*tert*-butyl-dimethyl-silyl)-β-D-maltosyloxy-methyl]-phenyl}- acetamide or a pharmaceutically acceptable salt thereof;

N-{2-Chloro-5-[([6,6'-di-*O*-benzoyl-β-D-maltosyl]oxy)methyl]phenyl}-acetamide or a pharmaceutically acceptable salt thereof;

N-{2-Chloro-5-[([6,6'-di-*O*-benzoyl-2,2',3,3',4'-penta-acetyl-β-D-maltosyl]oxy)-methyl]phenyl}-acetamide or a pharmaceutically acceptable salt thereof;

(4-Chloro-3-nitrophenyl)methyl-4-*O*-[6-*O*-(3-pyridinylcarbonyl)-α-D-glucopyranosyl]-β-D- glucopyranoside-6-(3-pyridinecarboxylate) or a pharmaceutically acceptable salt thereof;

(4-Chloro-3-nitrophenyl)methyl-4-*O*-[6-*O*-(3-pyridinylcarbonyl)-α-D-glucopyranosyl]-β-D- glucopyranoside or a pharmaceutically acceptable salt thereof;

N-[2-Chloro-5-[[(4-*O*-α-D-glucopyranosyl-β-D-glucopyranosyl)oxy]methyl] phenyl]-3- pyridinecarboxamide or a pharmaceutically acceptable salt thereof;

Benzoic acid 6-{4-chloro-3-[(pyridine-3-carbonyl)-amino]-benzyloxy}-4,5-dihydoxy-3- (3,4,5-trihydroxy-6-hydroxymethyl-tetrahydro-pyran-2-yloxy)-tetrahydro-pyran-2- ylmethyl ester or a pharmaceutically acceptable salt thereof;

5-{[6,6'-Bis-*O*-(4-toluenesulfonyl)- β-maltosyl]-oxy-methyl}-2-methyl-1-nitrobenzene or a pharmaceutically acceptable salt thereof;

5-{[2,2',3,3',4'-Penta-*O*-acetyl-6,6'-bis-*O*-(4-toluenesulfonyl)- β-maltosyl]-oxy-methyl}- 2-methyl-1-nitrobenzene or a pharmaceutically acceptable salt thereof;

5-{[6,6'-Dideoxy-6,6'-bis(4-nitro-imidazol-1-yl)- β-maltosyl]-oxy-methyl}-2-methyl-1- nitrobenzene or a pharmaceutically acceptable salt thereof; and

5-{[2,2',3,3',4'-Penta-*O*-acetyl-6,6'-dideoxy-6,6'-bis(4-nitro-imidazol-1-yl)- β-maltosyl]- oxy-methyl}-2-methyl-1-nitrobenzene or a pharmaceutically acceptable salt thereof.

Each of the compounds recited above are exemplified compounds of formula (I) in which variable Y is O. Other structural features present in this group of compounds are discussed in more detail below.

No new matter is introduced by these amendments.

Rejections under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 4 and 5 for failure to satisfy the enablement requirements of 35 U.S.C. § 112, ¶1. According to the Examiner (Office Action page 2):

> Claims 4-6 recite methods of treating or inhibiting proliferative disorders. Typically 'inhibition' is used regarding processes, such as the underlying mechanism causing a disorder, and 'prevention' or 'prophylactic treatment' is used regarding the disorder or disease, *per se*. In these claims, it would appear that 'inhibiting' is used to mean 'preventing.'
>
> Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prevention of hyperproliferative vascular disorders (such as restenosis), does not reasonably provide enablement for prevention of such disorders in the general population.

Applicants respectfully disagree with the grounds for the rejection. However, to expedite prosecution, claim 4 as currently amended is now directed to a method of "treating hyperproliferative vascular disorders" instead of "treating or inhibiting hyperproliferative vascular disorders." Likewise, claim 5 as currently amended is now directed to a method of "treating restenosis" instead of "treating or inhibiting restenosis." Applicants respectfully request that the rejection be reconsidered and withdrawn and not be applied to new claims 9-15, which are drawn to methods for the prevention of hyperproliferative vascular disorders (claims 9 and 14) and methods for the prevention of restenosis (claims 10 and 15), in which the hyperproliferative vascular disorders and restenosis follow vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation; and related methods for the treatment of hyperproliferative vascular disorders (claim 11) and restenosis (claims 12 and 13).

Claim 7 is rejected for failure to satisfy the enablement requirements of 35 U.S.C. § 112, ¶1. According to the Office (Office Action, pages 2-3):

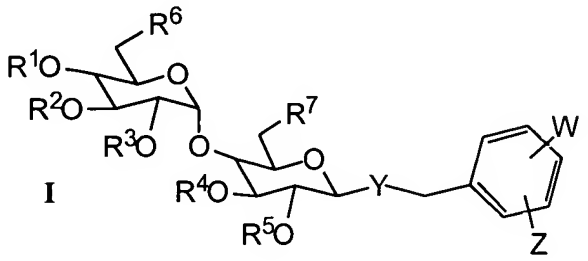
> The claims are drawn to the administration of the recited compounds for the inhibition of angiogenesis in various cancers. However, there is no indication that any of the compounds have anti-angiogenic activity. The only *in vitro* assay provided demonstrates the inhibition of proliferation of smooth muscle cells (SMCs), but this is not the accepted assay for angiogenic activity. As Applicant admits, agents such as heparin also inhibits proliferation of SMCs but promotes epithelial cell growth. See the paragraph bridging pages 1 and 2 of the instant specification. It is the inhibition (or growth promotion) of epithelial cell tissue that is the accepted model for determining anti-angiogenic (or angiogenic) activity. ... [I]t appears that one of ordinary skill in the art would require undue experimentation to determine which, if any, of the recited compounds would be useful for the inhibition of angiogenesis as set forth in the claims.

Applicants respectfully disagree with the grounds for the rejection. However, to expedite prosecution, Applicants have cancelled claim 7. Accordingly, the rejection of claim 7 is moot.

Rejection under 35 U.S.C. § 103

Claims 4-6 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nguyen et al., WO 96/14325 (Nguyen).

As discussed elsewhere, claims 4 and 5 as currently amended are directed to methods for the treatment of "hyperproliferative vascular disorders" and "restenosis," respectively. These methods include administering to a mammal in need thereof a benzylmaltoside compound of formula (I).



The benzylmaltoside compounds of the claims include a maltose group (left hand side of formula I) and a benzyl group (right hand side of formula I) that are linked *via* a divalent moiety Y. Claims 4 and 5 as currently amended require that the divalent moiety Y is S, NH, NMe, or CH_2.

Nguyen discloses methods for "treating diseases and conditions which are characterized by excessive smooth muscle proliferation, such as restenosis" (Nguyen, page 1, lines 6-8). Some of the Nguyen methods include administering a benzylmaltoside compound in which the divalent moiety corresponding to Y in Applicants' formula (I) is oxygen. Nguyen does not disclose or suggest compounds having a divalent moiety other than oxygen. Nguyen therefore does not disclose or suggest compounds meeting all of the compound limitations of the presently amended claims, nor does Nguyen disclose or suggest the use (or the desirability of using) of such compounds for the treatment of hyperproliferative vascular disorders and restenosis.

Applicants submit that claims 4 and 5 are not rendered obvious by Nguyen because Nguyen does not teach or suggest the modifications needed to arrive at Applicants' claimed methods, nor does Nguyen teach or suggest the desirability of making such modifications. As

such, a person of ordinary skill in the art would not have been motivated to modify the teachings of Nguyen to arrive at Applicants' claimed methods.

New independent claims 9 and 10 are directed to a method for the prevention of hyperproliferative vascular disorders and a method for the prevention of restenosis, respectively, in which the hyperproliferative vascular disorders and restenosis follow vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation. New claims 9 and 10 also require that the administered compound is a benzylmaltoside compound of formula (I) in which divalent moiety Y is S, NH, NMe, or CH_2. As such, new claims 9 and 10 are patentable over Nguyen for at least the reasons provided above.

Finally, as discussed elsewhere, new claims 11-13 are directed to methods for the treatment of hyperproliferative vascular disorders (claim 11) and restenosis (claims 12 and 13). New claims 14 and 15 are directed to a method for the prevention of hyperproliferative vascular disorders and a method for the prevention of restenosis, respectively, in which the hyperproliferative vascular disorders and restenosis follow vascular angioplasty procedure, vascular reconstructive surgery, or organ or tissue transplantation.

New claims 11-15 require that the administered compound is selected from a group of specific benzylmaltoside compounds in which Y is O and at least one of the following structural features is present:

(i) R^{13} is an amino acid or a benzoyl group that is further substituted with another benzoyl group (for purposes of clarification, R^{13} forms part of the substituent NHR^{13}, which is a group attached to the phenyl ring in the benzyl portion of the claimed benzylmaltoside compounds); or

(ii) each of R^1, R^2, R^3, R^4, and R^5 is hydrogen (i.e., the 2, 2', 3, 3', and 4' maltose hydroxyl groups are free or underivatized hydroxyl groups); or

(iii) R^6 and/or R^7 is a hydroxyl group that is derivatized with a *tert*-butyldimethyl silyl (TBDMS), benzoyl, pyridinylcarbonyl, or *p*-toluenesulfonyl (tosyl) group, or R^6 and R^7 are each 4-nitro-imidazol-1yl (i.e., the 6 and 6' maltose hydroxyl groups are either derivatized with a TBDMS, benzoyl, pyridinylcarbonyl, or tosyl group, or the 6 and 6' maltose hydroxyl groups are altogether replaced with the heterocycle, 4-nitro-imidazol-1yl).

Nguyen does not disclose or suggest compounds meeting all of the compound limitations of new claims 11-15. Specifically, Nguyen does not disclose or suggest the administration of benzylmaltoside compounds in which the substituent corresponding to R^{13} is an amino acid or a benzoyl-substituted benzoyl group. Further, the benzylmaltoside compounds administered in the Nguyen methods are those in which the maltose group is peracetylated (i.e., the 2, 2', 3, 3', 4', 6, and 6' maltose hydroxyl groups are all capped with an acetate ($CH_3C(O)$-) group); or the 2, 2', 3, 3', and 6 maltose hydroxyl groups are capped with an acetate group, $CH_3C(O)$-, and the 4' and 6' maltose hydroxyl groups form part of an isopropylidine group. Nguyen therefore also does not disclose or suggest the administration of benzylmaltoside compounds having the structural features delineated in (ii) and (iii) above. As such, new claims 11-15 are also patentable over Nguyen.

In view of the foregoing, Applicants respectfully request that the 35 U.S.C. 103(a) rejection based on Nguyen be reconsidered and withdrawn and not be applied to new claims 9-15.

Double Patenting

Claims 4-6 are rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claim 37 of commonly owned U.S. Patent 5,773,420 ("the '420 patent").

Claim 37 of the '420 patent is drawn to a method of treating restenosis, which includes the administration of the same benzylmaltoside compounds that are administered in the Nguyen methods. As discussed elsewhere, the benzylmaltoside compounds administered in the present claims are distinct and different from the benzylmaltoside compounds administered in Claim 37 of the '420 patent. Applicant submit that the present claims are patentable over claim 37 of the '420 patent for at least the reasons discussed above under the subheading "Rejection under 35 U.S.C. § 103" and therefore respectfully request that the rejection be withdrawn.

CONCLUSION

Applicants submit that all claims are in condition for allowance.

Enclosed is a $120 check for the One Month Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No.: 16156-040001.

Respectfully submitted,

Date: March 27, 2006

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